UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/809,621	06/02/97	IDA	N 599-158P

002292 HM22/1207
BIRCH STEWART KOLASCH & BIRCH
8110 GATEHOUSE ROAD
SUITE 500 EAST
FALLS CHURCH, VA 22042

EXAMINER	
CANELLA,K	
ART UNIT	**PAPER NUMBER**
1642	23

DATE MAILED: 12/07/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/809,621	Ida et al
Examiner	**Group Art Unit**
Karen Canella	1642

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3 months* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *13-16* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *13-16* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Please note that the examiner assigned to your application in the PTO has changed.

2. The request filed on 9/22/00, in Paper No. 22, for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/809,621 is acceptable and a CPA has been established. An action on the CPA follows.

3. Claims 7, 9 and 10 have been canceled. Claims 13, 14 and 15 have been amended. Claim 16 has been added. Claims 13-16 are examined on the merits.

Claim Objections

4. Claims 14 and 15 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. For reasons given in paragraph 6, below, claims 14 and 15 are read as being drawn to non-tumor-related bone disorders, therefore they fail to limit the scope of claim 13 which is drawn to tumor-related disorders. Further, for application of the prior art, claims 14 and 15 will not be considered as dependent on claim 13.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 is drawn to "tumor-related" bone disorders. Claims 14 and 15 recite genetic disorders and other disorders not related to bone diseases caused by tumor metastases. It is not clear if claims 14 and 15 are encompassing a method of treatment of an individual being afflicted

with both tumor-related and non-tumor related bone disorders simultaneously. For purpose of examination, claims 14 and 15 will be read as being drawn to non-tumor related bone disorders, and not dependent on claim 13.

Claims 13-15, recite "osteoclast-related bone disorder" further qualified by Markush groups consisting of diseases which have the potential to cause bone damage/detrioration. This is an improper Markush group since many of the listed diseases such as prostate cancer or hormonal disorders cannot be defined as an osteoclast-related bone disorder. Thus, many of the listed pathologies do not specify different species of osteoclast-related bone disorders, but specify potential causes of said disorders.

Claim 16 recites 10,000 to 10,000,000 units per day. The metes and bounds of this claim is unclear. For purposes of administration it is necessary to further specify the number of units/kg.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claim 13 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treatment of non-tumor related bone disorders, does not reasonably provide enablement for a method of treatment of tumor related bone disorders. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The specification provides data to support the use of interferons beta or gamma to inhibit bone resorption and promote mineralization in a murine model of menopausal osteoporosis. The specification provides no evidence that the administration of interferons beta or gamma would negate the deleterious effects of metastatic tumor cells in the bone. The specification provides data on the inhibitory effect of interferons beta and gamma on the formation of osteoclasts taken from normal bone under conditions which were not influenced by the proximity of tumor cells.

Sterns and Wang (Clinical and Experimental Metastasis, 1998, Vol. 16, pp. 693-702) teach that tumor cells, not osteoclasts, were primarily responsible for bone solubilization. There are no teachings in the specification to demonstrate that interferons beta or gamma could decrease or stop bone damage by tumor cells, or that osteolysis can be stopped independent of the tumor-cell derived stimulation of osteoclasts (Orr et al, Cancer, 2000, Vol. 88, pp. 2912-2918).

In addition, one cannot extrapolate the teaching of the specification to the claims because it is well known in the art that a significant problem associated with the use of interferons in therapy is development of resistance which results in the loss of sensitivity to target cells to such therapy (Kloke and Niederle, Cancer Treatment Reviews, 1990, vol. 17, pp. 81-88). It is clear that based on the state of the art, that the specification does not provide a treatment protocol which would minimize or avoid the development of interferon-associated resistance. In addition, the interferon may not be taken up by tumor infiltrated bone dues to fibrosis associated with the tumor metastases. If taken into the bone, the interferon may be inactivated by proteases secreted by the tumor cells and an efficacious local concentration may not be established. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict the efficacy of the claimed methods with a reasonable expectation of success. Given the lack of guidance in the specification, and the unpredictability in the art of cancer therapy, one of skill in the relevant art would be forced to undergo undue experimentation without a reasonable expectation of success, in order to practice the invention as claimed.

9. Claim 16 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 16 is drawn to a method of treatment of a bone disorder comprising the administration of interferon beta in a dosage range of 10,000 units per day to 10,000,000 units per day. The specification does not teach how many units/kg of interferon beta should be administered. The specification does not teach a dosage effective for treating bone disorders resulting from widely

differing pathologies. The specification does not teach the number of units of interferon beta/kg that is to be administered to a post-menopausal woman undergoing the treatment for osteoporosis. The specification does not teach the number of units of interferon beta/kg that is to be administered to a child undergoing treatment for a bone fracture. One of skill in the art would be forced into undue experimentation in order to find doses in units/kg body weight that would be effective for patients suffering from bone disorders resulting from widely differing pathologies.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

11. Claim 14 is rejected under 35 U.S.C. 102(b) as being anticipated by Rodriguiz et al (Pediatric Research, 1993, Vol. 33, pp. 384-389). Claim 14 is drawn in part to a method for treating a patient having an osteoclast-related bone disorder comprising the administration of interferon gamma, wherein the osteoclast-related bone disorder is osteopetrosis. Rodriguiz et al disclose a method of treating osteopetrosis comprising the administration of macrophage colony-stimulating factor and interferon gamma. Because claim 14 fails to further limit claim 13, it is not being considered as dependent on claim 13, therefore rejection over Rodriguiz has been applied only to claim 14.

12. Claim 16 is rejected under 35 U.S.C. 102(b) as being unpatentable over DelBianco and Sica (USP 5,024,833). Claim 16 is drawn to a method of treating a patient having a bone disorder, wherein the bone disorder is osteoporosis, comprising the administration of 10,000 to 10,000,000 units of interferon beta per day. Del Bianco and Sica disclose a method of treating patients having breast cancer comprising the administration of interferon beta at 10,000,000 units

per day. It is well known that women who have cancer of the breast often suffer from osteoporosis (Mincey et al, Mayo Clin Proc, 2000, Vol. 75, pp. 821-829), therefore, the treatment of osteoporosis is inherent in the treatment of breast cancer disclosed by Del Bianco and Sica.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

15. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brandely and Lando (USP 5,268,169) or Ammann (USP 4,944,941) or Sherwin (USP 4,851,219) or Adolf (4,791,101) in view of Roodman (Calcified Tissue International, 1993, Vol. 53, pp. S94-S98).). Claim 14 is drawn in part to a method for treating a patient having an osteoclast-related bone disorder comprising the administration of interferon gamma, wherein the osteoclast-related bone disorder is osteoporosis or Paget's disease of the bone. Brandely and Lando or Ammann or Sherwin teach methods of treatment for various neoplastic and respiratory diseases comprising the administration of gamma interferon. Adolf teaches a method of treatment for various neoplastic diseases comprising the administration of both gamma and beta interferons. Brandely

and Lando or Ammann or Sherwin or Adolf do not teach a method of treating a patient having osteoporosis or Paget's disease comprising administering gamma interferon. Roodman teaches that cytokines such as gamma interferon modulate the bone-resorbing process and normal calcium homeostasis and are therefore important in osteoporosis and Paget's disease of the bone. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to use the methods of treatment comprising the administration of gamma inteferon for the treatment of osteoporosis and Paget's disease of the bone. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Roodman on the ability of gamma interferon to inhibit osteoclast formation and osteoclast activity, the inhibition of which would be necessary in the treatment of osteoporosis and Paget's disease of the bone. Because claim 14 fails to further limit claim 13, it is not being considered as dependent on claim 13, therefore this rejection has been applied only to claim 14.

16. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over either of Brandely and Lando (USP 5,268,169) or Ammann (USP 4,944,941) or Sherwin (USP 4,851,219) or Adolf (USP 4,791,101), in view of Fujii et al (Calcified Tissue International, 1990, vol. 47, pp. 178-182). Claim 15 is drawn in part to a method for treating a patient having an osteoclast-related bone disorder comprising the administration of interferon gamma, wherein the osteoclast-related bone disorder is related to hyperparathyroidism. Brandely and Lando or Ammann or Sherwin teach methods of treatment for various neoplastic and lung diseases comprising the administration of gamma interferon. Adolf teaches a method of treatment for various neoplastic diseases comprising the administration of both gamma and beta interferons. Brandely and Lando or Ammann or Sherwin or Adolf do not teach a method of treating a patient having hyperparathyroidism related osteoclast bone disease comprising administering gamma interferon. Fujii et al teach the inhibition of hyperparathyroid related bone resorption by interferon gamma in vitro tissue culture. Fujii et al suggest that interferon gamma would be useful as a bone resorption inhibitor in vivo. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to use the methods of treatment comprising the

administration of gamma inteferon for the treatment of a patient having hyperparathyroidism related osteoclast bone disease. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Fujii et al on the ability of gamma interferon to inhibit bone resorption caused by a hyperparathyroid hormone, PTH, in vitro. Because claim 15 fails to further limit claim 13, it is not being considered as dependent on claim 13, therefore this rejection has been applied only to claim 15.

Conclusion

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

GEETHA P. BANSAL
PRIMARY EXAMINER

Karen A. Canella, Ph.D.
Patent Examiner, Group 1642
December 1, 2000